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Negative Nasopharyngeal and Oropharyngeal Swabs Do Not Rule Out COVID-19

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Coronavirus disease 19 (COVID-19) has become the Public Health Emergency of International Concern. A diagnosis is made by the detection of a novel virus or genetically similar coronavirus by molecular assay in clinical specimens (1). Nasopharyngeal and oropharyngeal (NP/OP) samples are commonly used as a screening tool. Here, we reported a case of COVID-19 pneumonia diagnosed from bronchoalveolar lavage (BAL) fluid that initially had negative tests from NP/OP swabs.

On 21 January 2020, a 28-year-old previously healthy Chinese man presented to Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand, with a 3-day history of high-grade fever and malaise. He also complained of rhinorrhea and cough, which had already resolved. He traveled from Jinzhou, China, to Chiang Mai on 15 January 2020 by trains and airplanes, with a brief transit in Wuhan, China. After his full itinerary was identified, his case was reported to the local government health agency as a patient under investigation for COVID-19. He was admitted to an airborne infection isolation room, and NP/OP swabs were obtained. The specimens were sent to two reference laboratories (the Thai Red Cross Emerging Infectious Diseases Health Sciences Center, Faculty of Medicine, Chulalongkorn University, and the Department of Medical Sciences, Ministry of Public Health) and tested negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by a real-time reverse transcriptase PCR (RT-PCR) assay (1). His chest radiograph on hospital day 3 did not reveal any infiltration. He continued to be febrile without other respiratory symptoms. On hospital day 5, the NP/OP swabs were repeated and were again reported as negative for SARS-CoV-2. On hospital day 7, he developed nonproductive cough. The chest radiograph revealed bilateral lower lung infiltrates with prominence on the right (Fig. 1), which was compatible with viral pneumonia. Bronchoscopy and BAL were performed on hospital day 8, and BAL fluid tested positive for SARS-CoV-2 by RT-PCR. On hospital day 10, his overall clinical condition improved, with increasing appetite, and he was afebrile. He was discharged on hospital day 18.

Our case highlighted the importance of high clinical suspicion in this epidemiologically matched patient who had negative NP/OP swabs. Although most of the reported cases have established diagnoses from NP/OP swabs, it is possible that NP/OP swabs could yield a false-negative result. Several factors might have contributed to the false-negative results, including, but not limited to, the sampling technique, transportation process, or limited gene(s) detection; however, it could also be explained by the nature of coronavirus itself. This finding was observed in previous severe acute respiratory syndrome (SARS) (2) and Middle East respiratory syndrome (MERS) (3) outbreaks. It is supported by the basic science evidence that the target functional receptor of these viruses is angiotensin-converting enzyme 2 (ACE2) (4, 5). Surface expression of ACE2 was found abundantly on both type I and type II alveolar epithelial cells but

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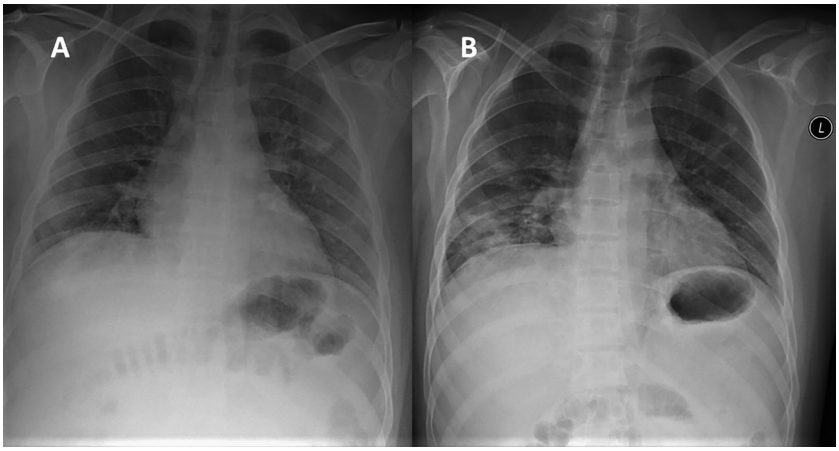

FIG 1 Chest radiographs. A posteroanterior radiograph of the chest in the upright position of the patient on hospital day 3 (A) shows no infiltration. A follow-up radiograph on hospital day 7 (B) after the patient developed nonproductive cough reveals new bilateral lower lung infiltrates, which are predominantly noticed on right lower lung zone.

minimally on bronchial epithelial cells and negative on the nasal, oral, and nasopharynx samples. Based on this case presentation, we strongly recommend that clinicians continue to be suspicious of COVID-19 infection in an epidemiologically linked patient despite a negative NP/OP result.

REFERENCES

1. World Health Organization. 2020. Novel coronavirus (2019-nCoV) technical guidance: laboratory testing for 2019-nCoV in humans. World Health Organization, Geneva, Switzerland. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance.
2. Peiris JSM, Chu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLM, Law KI, Tang BSF, Hon TYW, Chan CS, Chan KH, Ng JSC, Zheng BJ, Ng WL, Lai RWM, Guan Y, Yuen KY. 2003. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet 361:1767–1772. https://doi.org/10.1016/S0140-6736(03)13412-5.
3. Memish ZA, Al-Tawfiq JA, Makhdoom HQ, Assiri A, Alhakeem RF, Albarrak A, Alsubaie S, Al-Rabeeah AA, Hajomar WH, Hussain R, Kheyami AM, Almutairi A, Azhar EI, Drosten C, Watson SJ, Kellam P, Cotten M, Zumla A. 2014. Respiratory tract samples, viral load, and genome fraction yield in patients with Middle East respiratory syndrome. J Infect Dis 210:1590–1594. https://doi.org/10.1093/infdis/jiu292.
4. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. 2004. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 203:631–637. https://doi.org/10.1002/path.1570.
5. Wan Y, Shang J, Graham R, Baric RS, Li F. 2020. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. J Virol https://doi.org/10.1128/JVI.00127-20.